GREENLANE MEDICAL SPECIALISTS CME 21.02.18

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COUNTIES MANUKAU HEALTH

CASE

- 25 year old female patients
  - Alarm symptoms and high risk factors for colorectal cancer
  - Ethnicity
  - Algorithm for iron deficiency anaemia work-up
  - Safety of endoscopy during pregnancy
  - Use of CEA

CASE

- Ms K
- 25 year old Maori female
  - 2 kids

- Recent Gen Surg admission
- PR bleed. ? Haemorrhoidal bleed
- Lowest Hb 75

- What would you do next?

HISTORY: THE MORE THE BETTER

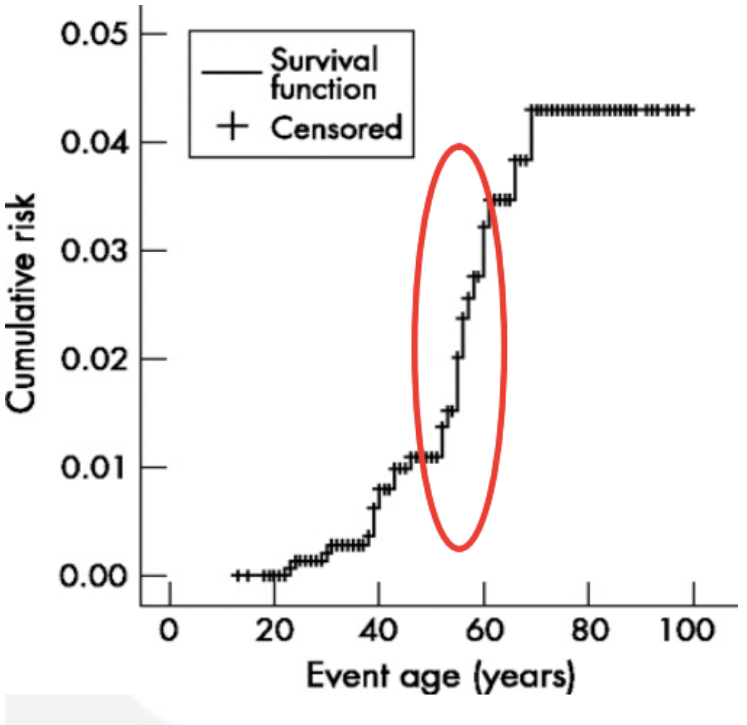
- Intermittent PR bleed
  - Fresh. Different shade of red
  - On tissue paper, in the toilet bowl,
  - Frequency
  - Volume
- One year
- Low abdominal pain
- Smoker
- Other symptoms?

ALARM SYMPTOMS

- PR bleed
- Unintentional weight loss
  - 5% of body weight or 4.5kg over 6 months
- Change of bowel habit- diarrhoea, thinning of the stool > constipation
- Severe unremitting symptoms
- Iron deficiency anaemia without apparent cause

HIGH RISK FACTORS: SOMETHING YOU CAN'T CHANGE

- Getting older. Especially above age 50
- Personal history of colorectal polyps or colon cancer
- Personal history of IBD, especially >8 years
- Family history of colon polyps or colon cancer
  - First degree relative <55
- Genetics <5%: FAP, Lynch, SSPS



HIGH RISK FACTORS: SOMETHING YOU CAN CHANGE

- Overweight/Obese
  - Especially larger waistline
  - Obesity BMI >29 RR 1.45
- Smoking: Cigarette smoking RR 1.18
- Diabetes: RR 1.38
- Physical inability: Physical Activity – 24% reduction
- Diet: BBQ meat, processed meat
  - 17% increase risk if > 100g red meat/day
  - 18% increased risk if >50g processed meat
- Heavy alcohol use: 4 drinks/day, RR 1.21

SYMPTOM PRESENTATIONS AND OTHER CHARACTERISTICS OF COLORECTAL CANCER PATIENT COLON IN THE SOUTH AUCKLAND POPULATION

Table 1. Demographics

Variables	European	Māori	Pacific	Asian	Total
Median age (years)	73.5	62.8	61.9	68.4	71.8
± IQR (years)	15.8	24.6	11.6	17.5	17.8
% Male	50.6	42.2	62.3	55	51.6
TNM stage (%)					
I	112 (18.3)	6 (13.3)	8 (10.4)	7 (11.7)	133 (16.7)
II	185 (30.2)	10 (22.2)	18 (23.4)	20 (33.3)	233 (29.3)
III	186 (30.2)	17 (37.8)	21 (27.3)	21 (35.0)	245 (30.8)
IV	111 (18.1)	12 (26.7)	29 (37.7)	10 (16.7)	162 (20.4)
Unknown	19 (3.1)	0 (0)	1 (1.3)	2 (3.3)	22 (2.8)
No surgery performed (%)	62 (10.1)	6 (13.3)	20 (26.0)	4 (6.7%)	92 (11.6%)
Inpatient cohort	233	21	37	19	310
Outpatient cohort	380	24	40	41	485
Total (%)	**613 (77.1)**	**45 (5.7)**	**77 (9.7)**	**60 (7.5)**	**795**

Symptom presentations and other characteristics of colorectal cancer patient Colon in the South Auckland population. NZMJ 2013

ETHNICITY

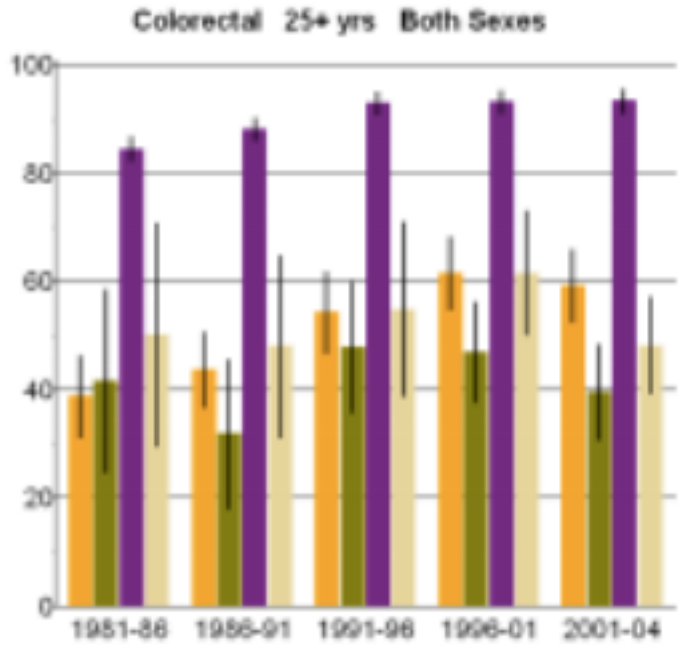


Figure 2. Age-standardised colorectal cancer incidence rate per annum (Jan 2006–Jan 2011)

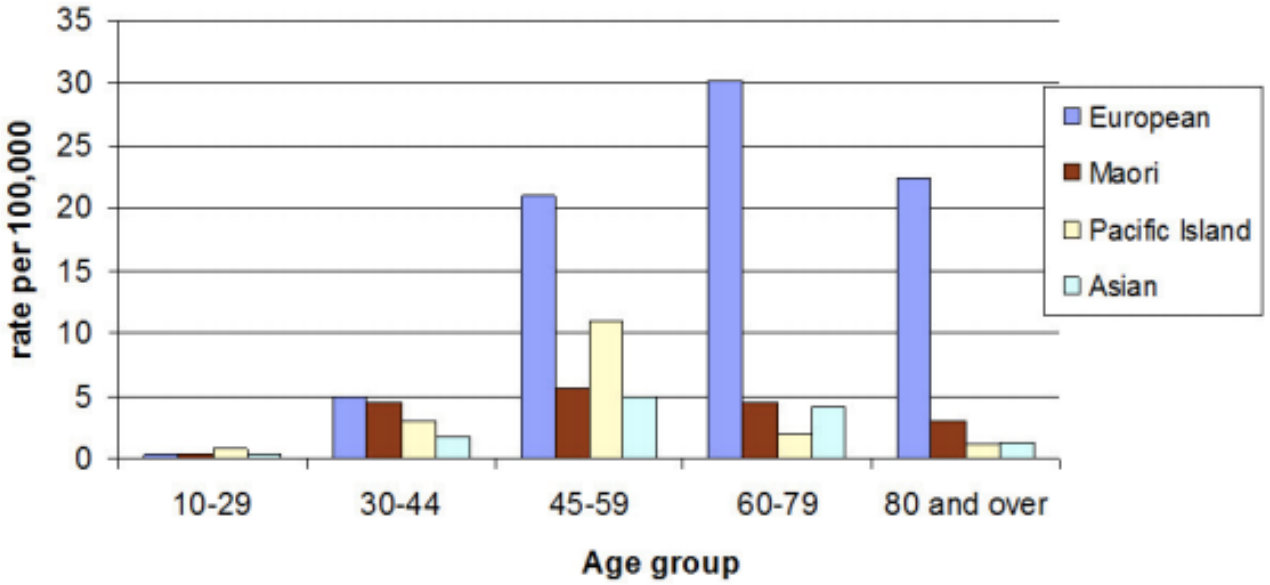


Table 2. Outpatient and inpatient cases characteristics (symptoms can be multiple; CIBH - change in bowel habit/diarrhoea)

Outpatient symptoms	European	%	Māori	%	Pacific	%	Asian	%	Total	%
Rectal bleeding	146	38.4%	12	50.0%	23	57.5%	24	58.5%	205	42.3%
CIBH	114	30.0%	6	25.0%	2	5.0%	8	19.5%	130	26.8%
Constipation	34	8.9%	4	16.7%	9	22.5%	3	7.3%	50	10.3%
Abdominal pain	63	16.6%	4	16.7%	7	17.5%	5	12.2%	79	16.3%
Weight loss	61	16.1%	7	29.2%	14	35.0%	7	17.1%	89	18.4%
Other symptoms (aggregated)	140	36.8%	4	16.7%	12	30.0%	18	43.9%	174	35.9%
Total	**380**		**24**		**40**		**41**		**485**	

Inpatient symptoms	European	%	Māori	%	Pacific	%	Asian	%	Total	%
Rectal bleeding	48	20.6%	4	19.0%	18	48.6%	9	47.4%	79	25.5%
CIBH	47	20.2%	8	38.1%	7	18.9%	2	10.5%	64	20.6%
Constipation	44	18.9%	5	23.8%	7	18.9%	2	10.5%	58	18.7%
Abdominal pain	109	46.8%	12	57.1%	17	45.9%	7	36.8%	145	46.8%
Weight loss	49	21.0%	6	28.6%	19	51.4%	7	36.8%	81	26.1%
Other symptoms (aggregated)		45.1%		33.3%		35.1%		26.3%		41.9%
Total	**233**		**21**		**37**		**19**		**310**	

Symptom presentations and other characteristics of colorectal cancer patient Colon in the South Auckland population. NZMJ 2013

CASE CONTINUE

- 25 year old Maori female
- Fresh PR bleed for one year ? Haemorrhoidal bleed
- Lowest Hb 75
- Some lower abdominal pain.

- O/E not unwell. BMI 37
- Distended abdomen. Non-tender
- PR: no blood on the glove. No mass palpated.

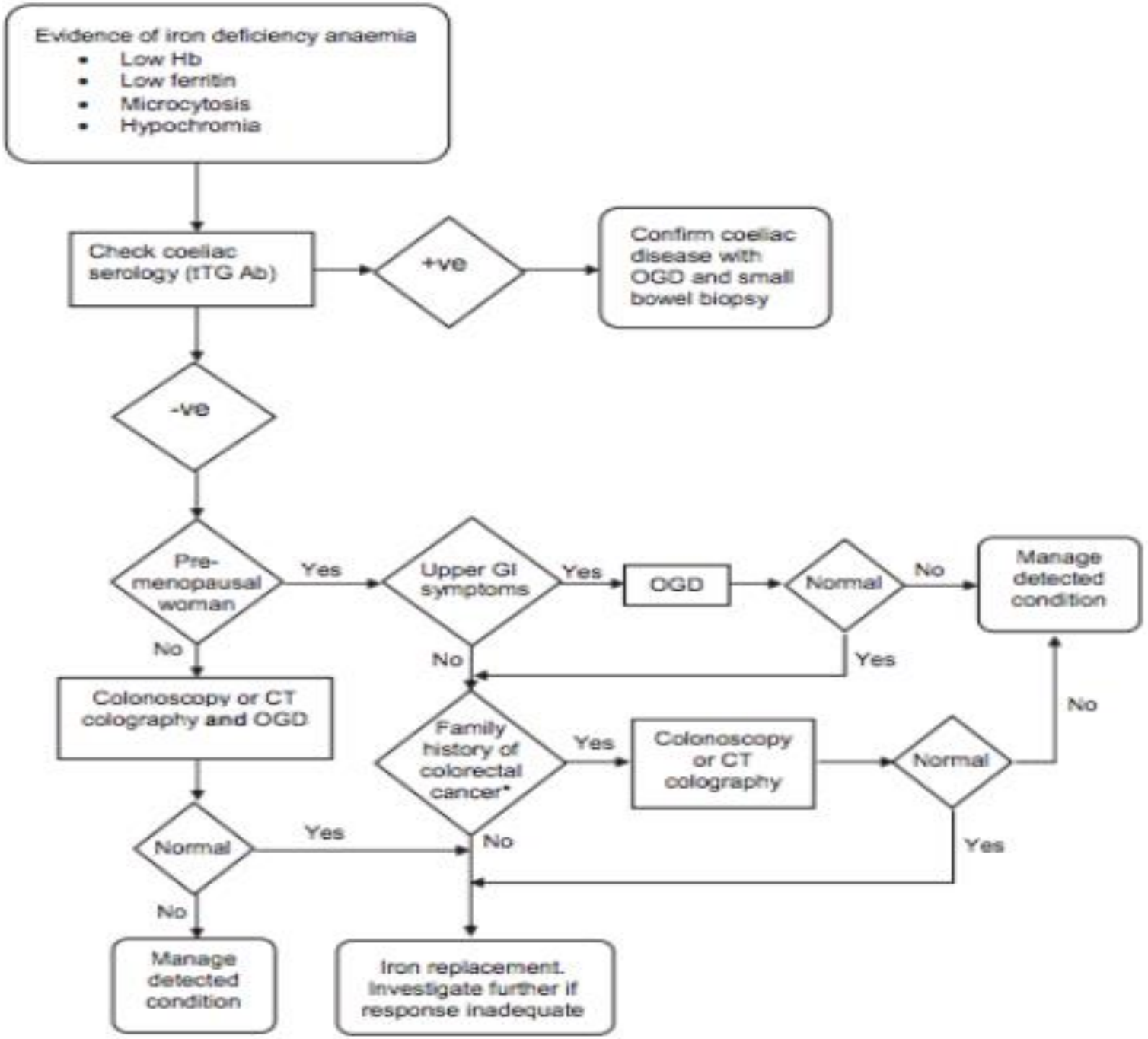
PRELIMINARY INVESTIGATION

- Hb75, MCV 72
- Ferritin 7
- Liver function: ALT 60, ALP 80, GGT 100
- Faecal spec –ve for infection

IRON DEFICIENCY ANAEMIA

- Ferritin <20, increase transferrin, increase TIBC, low transferrin sat, increase sTfR
- Common referral to Gastro department: 15%
- 5% in men and post-menopausal women
- Management
  - Identify the cause
  - Treat
  - Replace iron

Occult GI blood loss		Malabsorption		Non-GI loss	
Common		Common		Common	
• Aspirn/NSAID	10-15%	• Coeliac disease.	6%	• Mensturation.	30%
• Colon cancer	10%	• Gastrectomy	<5%	• Blood donation.	5%
• Gastric cancer.	5%	• H. Pylori	<5%		
• Benign gastric ulcer.	5%				
• Angiodysplasia	5%				
Uncommon		Uncommon		Uncommon	
• Oesophagitis	2-4%	• Gut resection.	<1%	• Haematuria	1%
• Oesophageal cancer.	1-2%	• Bacterial overgrowth.	<1%	• Epistaxis	1%
• GAVE	1-2%				
• Small bowel tumour.	1-2%				
• Cameron ulcers in hiatus.	<1%				
• Ampullary cancer	<1%				


Evidence of iron deficiency anaemia
Low Hb
Low ferritin
Microcytosis
Hypochromia
Check coeliac serology (tTG Ab)
+ve
Confirm coeliac disease with OGD and small bowel biopsy
-ve
Pre-menopausal woman
Yes
Upper GI symptoms
Yes
OGD
Normal
No
Manage detected condition
No
Yes
No
Colonoscopy or CT colography and OGD
Family history of colorectal cancer*
Yes
Colonoscopy or CT colography
Normal
No
Normal
Yes
No
Yes
No
Manage detected condition
Iron replacement. Investigate further if response inadequate

- Not Vegetarian
- Menorrhagia: 7/30. Heavy clots for first 4 days

WAIT, THERE IS MORE!!!

- " By the way, doc, something I need to tell you……
- " I AM PREGNANT, 10 weeks"
- And…." My bleeding is worse in the last 2 months…"

ENDOSCOPY IN PREGNANCY

- Not well-studied
- Risky
- Foetus is particularly sensitive to maternal hypoxia and hypotension
- Justified when it is clear that failure to perform the procedure could expose the mother/or foetus to greater risk
- IF it has to be done, defer to 2nd trimester

- Risk vs Benefit
  - Teratogensis
  - Premature labour

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SAFETY OF MEDICATIONS USED IN ENDOSCOPY

Category	Description
A	Well studied. Not increase risk
B	Animal study shows no harm. Not enough human study. *Or* Animal study shows harm. Human study shows failed to show risk
C	Animal study shows harm. No human study
D	Human study show harm

Lidocaine	**B**
Fentanyl	**C**
Midazolam	**D**
Naloxone	**B**
Flumazenil	**C**
Propofol	**B**
Bowel prep **- Sodium phosphate** **-polyethylene glycol**	**C or X**

GENERAL PRINCIPLES FOR ENDOSCOPY IN PREGNANCY

- Every procedure requires a pre-operative consultation with an obsterician
- Strong indication!!!
- Talk to the patient!
- Defer to second trimester if possible
- Use Category B drugs if possible
- Minimize procedure time
- Contraindicated in placental abruption, imminent delivery, ruptured membrane or uncontrolled eclampsia

TABLE 2. Indications for endoscopy in pregnancy
Significant or continued GI bleeding
Severe or refractory nausea and vomiting or abdominal pain
Dysphagia or odynophagia
Strong suspicion of colon mass
Severe diarrhea with negative evaluation
Biliary pancreatitis, symptomatic choledocholithiasis, or cholangitis
Biliary or pancreatic ductal injury

CARCINOEMBRYONIC ANTIGEN (CEA)

- Reference range: <3.0
- Glycoprotein
- Fetal tissue and colon cancer. Also present in healthy tissue
- Study of 700 apparently healthy volunteers
  - Male: Smokers 6.2 ug/L Non smokers 3.4 ug/L
  - Female: Smokers 4.9ug/L Non smokers 2.5ug/L

CEA may be elevated with the following carcinomas:

- Colorectal (70%)
- Pancreatic (55%)
- Gastric (50%)
- Lung (45%)
- Breast (40%)
- Uterine (40%)
- Ovarian (25%)

Benign conditions causing elevated CEA include:

- Cirrhosis (45%)
- Emphysema (30%)
- Rectal polyps (5%)
- Benign breast disease (15%)
- Ulcerative colitis (15%)

- Using an upper limit of normal of 2.5ug/L
- CEA sensitivity of 36% and specificity of 87% for screening for Duke's A and B colon cancer
- In unselected populations prevalence of CRC is low – PPV therefore is low and is of little value in screening healthy subjects
- CEA is raised in both adenocarcinoma as well as benign diseases

- Not a good screening tool

- Sensitivity in symptomatic patients is likely to be higher as they are more likely to have more advanced disease
- Symptoms and CEA > 5 x ULN should be considered strongly suggestive of cancer.

CARCINOEMBRYONIC ANTIGEN (CEA)

- Established disease
- Tumour stage
  - Eg Dukes A 28%, B 45% C 75% D 84% (CEA >2.5 hg/L)
  - If CEA >5 – A 3%, B 25%, C 45%, D65%
  - More like to have liver metastasis. Worse prognosis
- Tumour site
  - Left sided tumour produce more
- Tumour grade
  - Well-differentiated CRC produce more
  - Higher CRC grade not necessarily higher CEA

CEA FOR POST OPERATIVE RECURRENCE

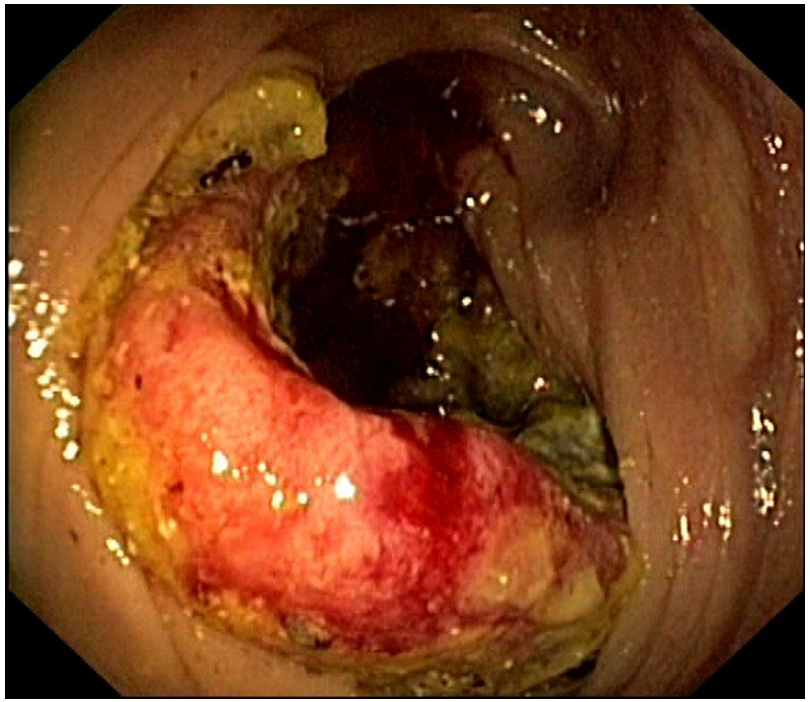
- Normalized!
- 85% recurrence happen in first 30months
- Aim is to detect recurrent disease at and early and treatable stage
  - Small and retrospective studies
  - However this seems to have a sensitivity of 80% (17-89%) and specificity of 70% (34-91%)
  - Most useful for detecting Liver Metastasis – sensitivity of 94%, specificity of 96% (one study 100% sensitivity)
  - Poor at detection of locoregional recurrence – however there has been a trial that shows superiority to endoscopy, CT and USS (?)
  - Monitoring recurrent CRC – lead time 5 months (4-10)
  - Cost-effective for the detection of potentially curable recurrent disease
- Recent UK study. Prospective study.
- 582 patients, 104 (17.9%) developed recurrence
- CEA > 5 – sensitivity 50% (95% CI: 40.1-59.9%),56 missed recurrences (53.8%)
  - 89 false alarms (56.7%) with 157 referred for further investigations – unnecessary investigations
- CEA >2.5 –missed recurrences 36.5%, false alarms 84%

- CEA must not used alone to monitor colon cancer recurrence.
- Good but not perfect – does not replace endoscopy and CT scan monitoring
- CEA every 3 months, colonoscopy one year post surgical resection.

- CEA is not recommended as a screening test
  - False positives
  - Leads to unnecssary investigations and anxiety
- If there are symptoms, further investigation is warranted anyway. Will doing CEA change your management?

CASE CONTINUE...

- Proceed to have flexible sigmoidoscopy on the same day
- Seen by surgeon 1 day after flexible sigmoidoscopy
- Staging: not CT. but chest xray and Abdominal MRI
- Day 6: Spontaneous miscarriage day6
- Day 6: CT: no distant metastasis
- Day 18: Anterior resection
- Post resection chemotherapy.
- Moving to Tauranga



TAKE HOME MESSAGE

- Take a full history
- Follow the algorithm
- Identify the alarm symptoms and high risk factors
- Maori and Pacific Islanders: not higher incidence but late diagnosis. Poor prognosis
- Endoscopy during pregnancy: postponed if clinically possible
- CEA: not recommended as screening tool

- Trust your gut feeling. If in doubt, ask a friend and refer!

QUESTION?